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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,686	11/28/2001	Klaus During	03528.0133.PCUS00	7122

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EXAMINER

HELMER, GEORGIA L

ART UNIT

PAPER NUMBER

1638

DATE MAILED: 09/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/889,686	Applicant(s) DURING ET AL.	
	Examiner Georgia L. Helmer	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 June 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>26 June 04, 16 June 05</u>
<u>04/21/04</u> | 6) <input type="checkbox"/> Other: _____ |

GA

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 16 June 2005 has been entered.

Status of the Claims

1. Applicant has requested cancellation of claims 1-18, and addition of new claims 19-29. Claims 19-29 are pending, and are examined in the instant action.
2. All rejections not addressed below have been withdrawn.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

4. Applicant's IDSs filed 26 April 2004 and 16 June 2005 are acknowledged and signed copies included herewith.

Claim Rejections - 35 USC § 112

5. Claim 19 and claims 20-29 dependent thereon, is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1, line 9, recites "said gas phase is rapidly displaced". The specification (p. 16, lines 4-6) indicates that the "air in the container was displaced rapidly by the" nitrogen, but does

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not define "rapidly". The term rapidly is a comparative term for which no relative basis is given. Accordingly the metes and bounds of "rapidly" are not apparent.

Claim Rejections - 35 USC § 112 Enablement

6. Claims 19-29 are rejected under 35 U.S.C. 112, first paragraph. This rejection is maintained for the reasons of record as set forth in the Office Action mailed 3 June 2004. Applicant has submitted amended claims 19-29 in place of the original claims, however the previous enablement rejection applies to the new claims, with the exceptions noted below. To the extent that the rejection was made to the scope of all "plants", the rejection is maintained. Only claim 29 is drawn to specific plants, wheat, barley, corn, sugar beet, sugar cane, potato, brassicaceae, tobacco and legumes; and potato is the exemplified plant.

Applicant's claims are drawn to a method for obtaining unspecified and any protein from a transgenic host plant, wherein the plant is unspecified and any plant, wherein the gene coding for the protein can be any and all proteins, wherein it is not expressed until said plant has been harvested, comprising (a) obtaining a transgenic host plant comprising a gene coding for a protein so that the gene is only expressed in the presence of a chemical inducer, (b) harvesting the transgenic host plant, (c) contacting the harvested plant with the chemical inductor in a reaction container via a gas phase surrounding the plant, wherein the gas in the gas phase is rapidly displaced by the chemical inductor in its gaseous form, and (d) isolating the protein. Dependent claims are drawn to various chemical inductors, inducible promoters inactive under aerobic conditions, to the GapC4 promoter, to the use of an inducible recombinase in

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the system and to transgenic host plants wheat, barley, corn, sugar beet, sugar cane, potato, brassicaceae, tobacco and legumes.

The 112.1 enablement rejection of record (Office Action 3 June 2004, p. 2-7) is applied to claims 19-29, for reasons of record, which are repeated in part below.

Applicant claims are drawn to any plant, any gene encoding a protein, and to any and all chemical inductors capable of existing in a gas phase, and any inducible promoter.

Working Examples: Applicant exemplifies a method of obtaining scFv antibody protein from a transgenic potato plant, where the transgenic construct uses the maize anaerobically inducible GapC4 promoter operatively linked to the cDNA which codes for an scFv antibody protein, where tissue is harvested and then is induced by treatment with anaerobic conditions for 40 hours (Example 1, pages 14-16, of the specification). Applicant teaches of use of inducible recombinase systems in the specification. Example 2, p. 16-18, is titled Recombination-mediated post-harvest production in transgenic potatoes.

Applicant traverses saying primarily that the specification lists a number of available inducible promoters (Response, p. 5). Applicant traverses saying primarily (Response, p. 6) that gaseous inductors suitable for use in the claimed method are described in the specification as are inducible promoters and their use in connection with chemical inducer are aptly discussed in the specification. Applicant's traversal is unpersuasive. Applicants list of inductors that can be used in the gas phase contains 2 examples: RH5992 (exemplified) and ethylene. Applicant lists inducible promoters

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suitable (specification p. 9 final ¶ bridging to p. 10); this listing of inducible promoters does not comprise adequate guidance for the claimed invention.

Applicant traverses saying primarily (Response, p. 5) that inducible promoters and chemical inducers are amply discussed in the specification, and that therefore neither the claimed inducers nor promoters requires trial and error experimentation. Applicant further asserts that their disclosure fully enables every element of the invention as presently claimed.

Applicant's traversal is unpersuasive. The unpredictability of the system as a whole (specific expression regulatory sequences + encoding the specific desired target protein + the specific plant + the specific tissue of the plant + environmental manipulation of the inducing conditions), which is the claimed invention, is the issue. Whereas a given step may function "perfectly", it is the success the sum of the steps which is required to enable the claimed invention of the system.

As set forth in the Office Action of 3 June 2004, in discussing the Wands factors, The state of the art and the unpredictability thereof, the state of the art of chemical control of gene expression is unpredictable (Gatz, Chemical Control of Gene Expression, Annu. Rev. Plant Physiol. Plant Mol. Biol., vol. 48, pages 89-108, 1997, see p. 99, 1st full ¶, and 104, 2nd full ¶). The state of the art of post harvest production systems for production of desired proteins in plants is that the systems which have been described are systems based on the wounding of plant material, which is a system which is inducible/induced in both pre- and post-harvest conditions (specification p. 2, 1st full ¶).

Claim Rejections - 35 USC § 102

7. Claims 19-24 and 28-29 are rejected under 35 U.S.C. 102(e) over US 6,194,201 B1 issued 27 February 2001, with a 102(e) date of 27 October 1998, for reasons of record. This rejection is maintained for the reasons of record as set forth in the Action mailed 3 June 2004. Applicant's arguments filed 01 September 2004 have been fully considered, but are not deemed persuasive.

Applicant traverses saying primarily (Response, p. 5) that claim 19 recites a harvested plant being contacted with an inductor in a reaction container via a gas phase surrounding the harvested plant, the gas phase being rapidly displaced by a chemical inductor in its gaseous form. Applicant further asserts that because the '201 patent does not teach the reaction container as claimed, nor the rapid displacement of the gas phase, it cannot anticipate claim 19.

Applicant's traversal is unpersuasive. Applicant asserts that the gas phase in the Anaerocult system is displaced over several hours, that such displacement is consistent with the teaching of other prior art that only gradual but not rapid displacement leads to the hypoxic acclimation necessary for metabolism giving rise to production of proteins. Applicant asserts that the prior art teachings do not suggest rapid displacement of the gas phase. US 6,194,201 teaches (column 3, lines 48-62) the anaerobic induction of plant tissue incubated in an air-tight glass container with Anaerocult A. This is exemplified in Applicant's specification (p.14-16) as well as in the '201 patent. Furthermore, see above, Claim 19 and claims 20-29 dependent thereon, is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to

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particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 19, line 9, recites "said gas phase is rapidly displaced". The specification (p. 16, lines 4-6) indicates that the "air in the container was displaced rapidly by the" nitrogen, but does not define "rapidly". The term "rapidly" is a comparative term for which no relative basis is given. Accordingly the metes and bounds of "rapidly" are not apparent.

Applicant traverses saying primarily (Response, p. 6) that the Examiner erred in considering column 4, lines 31-36 of the '201 patent as the alleged evidence for a post harvest production system in sliced potato tubes, saying not anaerobic post harvest production system was show, not deoxidizing of the gas phase, no protein was detected or isolated.

Applicant's traversal is unpersuasive. The previous claims have been cancelled. The present claims are anticipated by the '201 patent (column 3, lines 48-62), which teaches a method for obtaining any protein from a transgenic host plant, wherein the plant is unspecified and any plant, wherein the gene coding for the protein can be any and all proteins, wherein it is not expressed until said plant has been harvested, comprising (a) obtaining a transgenic host (potato) plant ('201, column 3, line 53) comprising a gene coding for a T4-lysozyme protein so that the gene is only expressed in the presence of a chemical inducer (anaerobic conditions) ('201, column 3, line 48-49), (b) harvesting the transgenic host plant ('201, column 3, line 59), (c) contacting the harvested plant with the chemical inductor in a reaction container via a gas phase surrounding the plant ('201, column 3, line 59-62), wherein the gas in the gas phase is

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rapidly displaced by the chemical inductor in its gaseous form, and (d) isolating the protein. In the process of the anaerobic induction, the plant tissue is placed in the reaction vessel ('201, column 3, line 59-62) and induced. The desired protein produced upon induction of anaerobic conditions is thus isolated away from plant tissue which has not been induced. Since no statement is made of what the isolated protein is isolated from, this physical separation is interpreted to mean "isolated".

Applicant traverses saying primarily (Response, p. 7) the term "post harvest production" refers to induction of expression of foreign proteins after harvest, and the term "harvest" refers to removal of the plant or part of it from its previous growing environment. Applicant's traversal is unpersuasive. "Post harvest production" is not defined in the specification. In the lack of a specific definition of "post-harvest", the term is given its broadest reasonable meaning. Webster's gives the meaning of "harvest" as being a gathered crop, and "post" means "after", therefore post-harvest is taken to mean a crop after being gathered.

Accordingly '201 anticipates the claimed invention.

Claim Rejections - 35 USC § 103

8.

9.

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10. Claims 19-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,194,201 as applied to claims 19-24 and 28-29 above, and further in view of WO 95/00555 (5 January 1995).

11.

US 6,194,201 do not teach a method using a LBD (ligand binding domain) recombinase system.

WO 95/00555 (hereafter '555) teaches a method using a LBD (ligand binding domain) recombinase system (p. 3, 1st and 2nd full ¶s) where inducible recombinase is FLP recombinase translationally fused to the Estrogen LDB and where the recombinase is not active until the Estrogen LBD is bound to its receptor in the nucleus (Figure 1B).

WO 95/00555 provides motivations to combine use of the LBD-recombinase system with the method of obtaining a desired protein of US 6,194,201 (Abstract) saying that the LBD-recombinase system provides a practical means to regulate recombinase in cells and organisms.

Given the recognition of one of ordinary skill in the art of the value of using the claimed invention in harvested plants, one of ordinary skill in the art would have been motivated to use gene expression in post-harvest potato as taught by US 6,194,201, in combination with the LBD recombinase system of WO 95/00555 in order to regulate and activate the availability of the anaerobic gene expression to produce T-4 lysozyme in post-harvest transgenic potato. Thus the claimed invention would have been prima facie obvious as a whole to one of ordinary skill in the art at the time it was made. Accordingly, the claimed invention is prima facie obvious in view of the prior art.

RE: Claim 24 and 28. The language "induced by compensating the functional inhibition of the transcription and/or translation" is unclear and ambiguous. Therefore the Examiner interprets these terms to mean turning expression "on" from an "off" state, which is what happens when anaerobic conditions induce the GapC4 promoter to express the lysozyme protein.

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Remarks

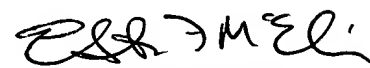
12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Georgia L. Helmer whose telephone number is 571-272-0796. The Examiner can normally be reached on M-Th, 10:30am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on 571-272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Georgia Helmer PhD
Patent Examiner
Art Unit 1638- Transgenic Plants
15 September 2005


ELIZABETH MCELWAIN
PRIMARY EXAMINER